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Pollution Prevention and Toxics (7407)
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OPPT Chemical Fact Sheets

Acrylonitrile Fact Sheet: Support Document
(CAS No. 107-13-1)

This summary is based on information retrieved from a systematic search limited to secondary sources (see Appendix A). These sources include online databases, unpublished EPA information, government publications, review documents, and standard reference materials. No attempt has been made to verify information in these databases and secondary sources.

I. CHEMICAL IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

The chemical identity and physical/chemical properties of acrylonitrile are summarized in Table 1.

TABLE 1. CHEMICAL IDENTITY AND CHEMICAL/PHYSICAL PROPERTIES OF ACRYLONITRILE

Characteristic/Property	Data	Reference
CAS No.	107-13-1	
Common Synonyms	AN; acrylon; carbacryl; cyanoethylene; 2–propenenitrile; vinyl cyanide	U.S. EPA 1994
Molecular Formula	C_3H_3N	
Chemical Structure	CH_2=CH-C≡N	
Physical State	liquid	Budavari et al. 1989
Molecular Weight	53.06	
Melting Point	–83.55°C	Budavari et al. 1989
Boiling Point	77.3°C @ 760 mm Hg	Budavari et al. 1989
Water Solubility	73 g/L (20°C)	Budavari et al. 1989
Density	$d^{25/4}$, 0.8004	Budavari et al. 1989
Vapor Density (air = 1)	0.25	Leo and Hansch 1985
K_{OC}	9 (calculated)	CHEMFATE 1994
Log K_{OW}	–0.92 (measured)	CHEMFATE 1994
Vapor Pressure	108.5 mm Hg @ 25°C	CHEMFATE 1994
Reactivity	flammable and explosive (3.05 to 17.0% in air @ 25°C)	Budavari et al. 1989
Flash Point	0°C (open cup)	Budavari et al. 1989
Henry's Law Constant	8.8×10^{-5} atm·m^3/mole	U.S. EPA 1985
Fish Bioconcentration Factor	1.68 (measured)	CHEMFATE 1994
Odor Threshold	40.4 mg/m^3, average	IPCS 1983
Conversion Factors	1 ppm = 2.17 mg/m^3 1 mg/m^3 = 0.4605 ppmdelay	IPCS 1983

II. PRODUCTION, USES, and TRENDS

A. Production

Mannsville (1994) identified five producers of acrylonitrile in the United States in 1992: BP Chemicals; Cytec Industries; DuPont Company; Sterling Chemicals, Inc.; and Monsanto Company. In 1994, the estimated total capacity of acrylonitrile production in the United States is 3,080 million pounds (Mannsville 1994). Table 2 shows the producers, plant locations, and plant capacities of acrylonitrile in 1994.

The 1992 United States production volume of acrylonitrile was almost three billion pounds (see Tables 3 and 5).

TABLE 2. PRODUCERS OF ACRYLONITRILE AND THEIR CAPACITIES

Producer	Location	1994 Capacity (Millions of Pounds)
BP Chemicals	Green Lake, TX	700
BP Chemicals	Lima, OH	500
Cytec Industries	Fortier, LA	320
DuPont	Beaumont, TX	380
Monsanto	Chocolate Bayou, TX	480
Sterling Chemicals	Texas City, TX	700
TOTAL		3,080

Source: Mannsville 1994.

TABLE 3. PRODUCTION AND SALES VALUE OF ACRYLONITRILE IN 1992

Production	Sales Quantity	Sales Value	Average Unit Value
2,822,930	1,760,191	488,225	$3.61
(1,000 lb)	(1,000 lb)	($1,000)	(Per lb)

Source: USITC 1994.

B. Uses

Acrylonitrile monomer is a chemical intermediate used in the production of acrylic fibers, plastics, rubber elastomers, and other materials. It also undergoes reactions to form compounds used as solvents, polymeric materials, plasticizers, and intermediates for dyes, pharmaceuticals, and insecticides. AN is used to produce adiponitrile, a nylon intermediate, and acrylamide.

Styrene-acrylonitrile (SAN) and acrylonitrile-butadiene-styrene (ABS) are high-impact resins derived from AN. SAN resins are used in appliances, automotive, houseware, and packaging applications. ABS resins are used in appliances, business machines, telephones, transportation, recreation, luggage, and construction applications. These resins have been losing market share to other plastics. However, there is potential for growth in other acrylonitrile-based resins.

Nitrile rubbers are used in automotive fuel lines, while nitrile elastomers are used as latex coatings for oil resistant papers, leather, and textiles. Polyacrylonitrile (PAN), as a precursor for carbon fiber, is used in high-strength applications including aircraft parts and golf club shafts (Mannsville 1994). This market has been growing rapidly over the past few years, but remains highly specialized and low volume.

TABLE 4. END USE PATTERN OF ACRYLONITRILE--1994 ESTIMATE

Derivative (Typical Standard Industrial Classification (SIC) Code)[1]	Percent
Acrylic and Modacrylic Fibers (production, SIC 2824)	57
ABS Resins (production, SIC 2821)	23
Adiponitrile (production, SIC 2869)	8
Acrylamide (no applicable SIC code)	4
SAN Resins (production, SIC 2821)	3
Miscellaneous (includes nitrile elastomers) (production, SIC 2822)	5

Source: Mannsville 1994.

[1] The Standard Industrial Classification (SIC) code is the statistical classification standard for all Federal economic statistics. The code provides a convenient way to reference economic data on industries of interest to the researcher. SIC codes presented here are not intended to be an exhaustive listing; rather, the codes listed should provide an indication of where a chemical may be likely to be found in commerce.

C. Trends

Demand for acrylonitrile is expected to grow at an average annual rate of 2 to 3 percent after the 1990/1991 market slowdown. It is estimated that production was roughly 2,926 million pounds in 1994 (see Table 5). Exports were expected to increase from 1,020 million pounds in 1993 to 1,450 million pounds in 1994. U.S. capacity greatly exceeds domestic demand. About 40 percent of U.S. production of acrylonitrile was exported in 1993. Increasing worldwide capacity for AN production may limit U.S. exports in the future.

TABLE 5. ESTIMATED U.S. PRODUCTION AND CAPACITY OF ACRYLONITRILE (Millions of Pounds)

Year	1991	1992	1993	1994 (Projected)	1996 (Projected)
Capacity	3,080	3,080	3,080	3,080	3,200
Production	2,642	2,823	2,504	2,926	N/A
Exports	1,300	1,365	1,020	1,450	N/A
Demand	1,342	1,458	1,484	1,476	1,550

N/A: Not available
Source: Mannsville 1994.

III. ENVIRONMENTAL FATE

A. Environmental Release

Acrylonitrile apparently does not occur naturally (Howard 1989). Sources of release of acrylonitrile to the environment include fugitive emissions from facilities producing and using the chemical in the manufacture of acrylic and modacrylic fibers, ABS and SAN resins, adiponitrile, acrylamide, and other resins and chemicals. Small amounts of acrylonitrile have been detected in cigarette smoke and auto exhaust. AN may also be released from polyacrylic fibers and plastics (Howard 1989).

Acrylonitrile has been detected in the workplace and in the ambient atmosphere as a result of industrial releases (U.S. EPA 1985). Concentrations measured include: 3 to 20 mg/m^3 (1.4 to 9.2 ppm; air of an acrylic fiber plant), 1 to 325 $micrograms/m^3$ (0.46-150 ppb, near industrial plants), and levels of 0.5 to 2 ppm and 54 ppm (offgases from oil shale retort processing). Acrylonitrile has also been detected in cigarette smoke (1-2 mg/cigarette) (U.S. EPA 1985).

In 1992, environmental releases of the chemical, as reported to the Toxics Release Inventory by certain types of US industries, totaled about 5.5 million pounds, including 1.6 million pounds to the atmosphere, 3.9 million pounds to underground injection sites, 8 thousand pounds to land, and 1.5 thousand pounds to surface water (TRI92 1994).

B. Transport

If released to air, acrylonitrile is likely to remain long enough (see section III.C.1) so that dispersion of the chemical is expected to occur (Howard 1989). The removal of significant amounts of acrylonitrile from the atmosphere by wet (e.g., rain) and dry deposition is unlikely (U.S. EPA 1985).

In water, volatilization is a potential transport mechanism for acrylonitrile, but probably proceeds slowly as is indicated by its Henry's law constant (8.8×10^{-5} $atm{\cdot}m^3/mole$, calculated from the chemical's vapor pressure and water solubility at 25°C) (U.S. EPA 1985). Based on the overall transfer coefficient for acrylonitrile relative to oxygen, 0.59, and the reaeration rates for oxygen in typical bodies of water, the estimated volatilization half-lives of acrylonitrile in a typical pond, river, and lake are 6, 1.2, and 4.8 days, respectively (Howard 1989). The low log K_{OW} and high water solubility of acrylonitrile indicate that its adsorption to sediment and suspended particles would be minimal (U.S. EPA 1985).

In soil, acrylonitrile is volatile and not strongly adsorbed (K_{OC}, 9). The chemical will either volatilize rapidly or partition into the soil's water fraction. In soil water, the chemical could leach into groundwater or be transported in water runoff (U.S. EPA 1985).

C. Transformation/Persistence

1. Air —If released to the atmosphere, acrylonitrile will degrade by reaction with atomic oxygen (half-life not available, but as a group, olefins react with atomic oxygen faster than any other class of compounds) and hydroxyl radicals (half-life, 2 days @ 25°C)(U.S. EPA 1985).

2. Water — The main removal pathways for acrylonitrile in water are evaporation and biodegradation; both proceed slowly (U.S. EPA 1985). Photolysis and hydrolysis are not expected to be significant fate processes (U.S. EPA 1985). Acrylonitrile evaporates from water with a half-life of 1 to 6 days. AN was biodegraded within one week in receiving water containing acclimated microorganisms. Biodegradation values (reported in Howard 1989) determined for acrylonitrile under aerobic conditions are as follows:

- >95% using activated sludge inocula after 21 days of acclimation (>70% theoretical BOD removal);
- 30% of theoretical BOD removal after 10 days in a treatment plant;
- >99% degradation in bench-scale continuous flow reactor (30% of theoretical BOD removal);
- 0 and 38% of theoretical BOD removal after 5 and 20 days, respectively; and

- complete degradation in 7 days in a screening study with sewage seed.

Acrylonitrile degraded in 6 days in Mississippi River water and in 20 days in another study in river water. Limited data indicate that the chemical is amenable to biodegradation under anaerobic conditions, but only at low concentrations; high concentrations may be inhibitory to some anaerobes (U.S. EPA 1985).

3. Soil — In soil the most likely fate of acrylonitrile is evaporation. The K_{OC} for acrylonitrile is 9 (calculated from water solubility), indicating that adsorption to soil will not be significant (Howard 1989). The biodegradability of acrylonitrile in water suggests that some biodegradation may occur in soil.

4. Biota — The potential for the bioconcentration of acrylonitrile in aquatic organisms is low (U.S. EPA 1985). The bioconcentration factor for a bluegill exposed to acrylonitrile for 28 days in a continual flow apparatus, or until equilibrium was reached, was 48; the bioconcentration factor estimated from its water solubility is 1 (U.S. EPA 1985).

IV. HEALTH EFFECTS

A. Pharmacokinetics

1. Absorption — Acrylonitrile is absorbed by the inhalation, oral, and to some extent, dermal routes (U.S. EPA 1985). In experiments with human volunteers exposed by inhalation to 5 or 10 mg/m^3 (2.3 or 4.6 ppm) acrylonitrile, 52% of the inhaled dose was absorbed by the lungs (ATSDR 1990). In rats exposed to 4 mg/kg (note: exposure was by inhalation, but the concentration was reported in mg/kg) 2,3-^{14}C-acrylonitrile, the absorption of acrylonitrile was biphasic, characterized by a rapid dose-dependent phase that was followed by a slower dose-independent phase (ATSDR 1990). Male Sprague-Dawley rats were exposed for six hours in a "nose-only" chamber to acrylonitrile concentrations of 5 and 100 ppm (11 and 217 mg/m^3). The estimated total absorbed doses of 0.7 and 10.2 mg/kg for the 5 and 100 ppm concentrations indicate that about 41% and 30%, respectively, of inhaled radioactivity are absorbed (U.S. EPA 1987).

   For male Sprague-Dawley rats given oral doses of 0.1 and 10 mg/kg ^{14}C-acrylonitrile, recovery from body fluids, tissues, and excretions was 83% and 104% for the respective doses, indicating that absorption was nearly complete by the oral route (U.S. EPA 1985).

   The dermal absorption rate for human volunteers was estimated to be 0.6 mg/cm^2/hour (ATSDR 1990). A case study in which the accidental spraying of a man with acrylonitrile resulted in marked symptoms of toxicity indicated that significant quantities of acrylonitrile were absorbed through the skin (ATSDR 1990). The extent of absorption of acrylonitrile vapor through the skin of rabbits was 1% of that absorbed through the lungs (U.S. EPA 1985).

2. Distribution — Following a single oral or intravenous dose of 0.1 and 10 mg/kg radiolabeled acrylonitrile to rats, the parent compound and its metabolites were distributed to all tissues examined (U.S. EPA 1985). Regardless of route of exposure or dose, high levels of radioactivity occurred in the stomach, skin and red blood cells. The accumulation of label in the stomach following both intravenous and oral administration of ^{14}C-acrylonitrile suggest that enterogastric circulation may be important in the preferential localization of acrylonitrile in the stomach (ATSDR 1990). Whole-body autoradiography in rats and monkeys demonstrated localization of radiolabel in the liver, kidney, lung, adrenal cortex and stomach (ATSDR 1990).

   One hour after inhaling radiolabeled acrylonitrile, animals displayed measurable amounts of radiolabel in the brain, stomach, liver, kidney, lung and blood (ATSDR 1990).

3. Metabolism — The metabolites of acrylonitrile are the same in humans and in animals (ATSDR 1990). Animal studies indicate that metabolism occurs by the same pathways whether exposure is by the oral or the inhalation route (ATSDR 1990). Acrylonitrile can be directly conjugated to glutathione and excreted in urine as cyanoethylmercapturic acid or it can bind to other macromolecules. AN can also be metabolized by the microsomal enzyme system to 2-cyanoethylene oxide, which either reacts directly with tissue macromolecules or can be further metabolized to products that release cyanide. Cyanide is converted to thiocyanate and excreted in the urine or metabolized to carbon dioxide and eliminated through the lungs.

   The preferred pathway for the metabolism of acrylonitrile in humans and in animals appears to be conjugation with glutathione. However, in the event of glutathione depletion or if the pathway is overloaded (as may occur with high doses), metabolism of acrylonitrile in humans to thiocyanate via 2-cyanoethylene oxide is increased. 2-Cyanoethylene oxide reacts with cellular macromolecules and may be responsible for the carcinogenic effects of acrylonitrile (ATSDR 1990).

4. Excretion — In rats given oral doses of acrylonitrile, the primary route of excretion is via the urine, either as thiocyanate or other products of conjugation. Within the first 24 hours of a single oral dose, 40% to 60% was recovered in the urine (ATSDR 1990). Ten days after a single oral dose, 61% had been excreted in the urine, 3% in the feces, and 13% in expired air; 25% remained in the body covalently bound to the tissues (ATSDR 1990).

   In human volunteers, the elimination of inhaled acrylonitrile followed first-order kinetics, with a half-life of seven to eight hours (ATSDR 1990). The primary routes of excretion are in the urine and in expired air as CO_2. The excretion of acrylonitrile in the urine is dose related (the higher the exposure concentration, the larger the urinary recovered fraction). Fecal excretion of AN is a minor route following low and high doses.

B. Acute Effects

The symptoms of acute toxicity for acrylonitrile may resemble those of cyanide. Concentrations of acrylonitrile that are mildly irritating to adults have been fatal to children. Workers exposed to moderate to high concentrations have reported irritation, nausea, anemia, leukocytosis, renal effects, and mild jaundice, most of which abated when exposure ceased. Lethality data indicate that the chemical is moderately toxic to animals; it also causes severe damage to the skin.

1. Humans — In several instances, children have died in the presence of acrylonitrile vapors, whereas adults exposed under the same conditions experienced only mild irritation (U.S. EPA 1994). In one case, the child was sleeping in a room fumigated with acrylonitrile. Symptoms described in the child prior to death included respiratory malfunction, lip cyanosis, and tachycardia.

   Workers exposed to acrylonitrile concentrations of 16 to 100 ppm for 20 to 45 minutes in a synthetic rubber manufacturing plant experienced irritation of the mucous membranes, nausea, headaches, and nervous irritability (U.S. EPA 1994). For dose comparison purposes, the concentration of 16 ppm for a 20 minute exposure period converts to an oral dose of approximately 0.21 mg/kg[1]. Other observed effects, including low grade anemia, leukocytosis, renal effects, and mild jaundice, abated when exposure ceased.

   A man sprayed accidentally with acrylonitrile, incurring mostly dermal exposure, showed signs of poisoning from cyanide, a metabolite of acrylonitrile (ATSDR 1990).

2. Animals — Oral LD_{50} values for acrylonitrile in the rat range from 72 to 186 mg/kg (IPCS 1983). Oral LD_{50} values for other species range from 25 mg/kg for the mouse to 85 mg/kg for the guinea pig (IPCS 1983). Four-hour LC_{50} values are 470 mg/m^3 (216 ppm) for the rat, 300 mg/m^3 (138 ppm) for the mouse, and 990 mg/m^3 (456 ppm) for the guinea pig (IPCS 1983). Application of acrylonitrile to the skin of rabbits and guinea pigs resulted in erythema and necrosis; extensive dermal exposure may be lethal (IPCS 1983). The undiluted chemical is mildly irritating to the eye (IPCS 1983).

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[1]To approximate a route to route dose comparison, the following conversion of inhalation to oral dose (mg/kg/day) has been done: mg/m^3 x air breathed/20 min (m^3) x 1/body weight = dose (mg/kg/day); = 35 mg/m^3 x 0.42 m^3/20 min. x 1/70 kg = 0.21 mg/kg/20 min., assuming 10 m^3 breathed/8 hours and 100% absorption.

C. Subchronic/Chronic Effects

The EPA has derived an inhalation reference concentration (RfC[2]) of 0.002 mg/m^3 for acrylonitrile, based on degeneration and inflammation of nasal epithelium and hyperplasia of mucous secreting cells in rats exposed to 20 ppm for 2 years (U.S. EPA 1994).

1. Humans — The results of studies in humans with long-term exposure to acrylonitrile have been either negative or inconclusive for noncancer chronic effects (U.S. EPA 1994).

2. Animals — A chronic inhalation RfC of 0.002 mg/m^3 has been derived for acrylonitrile, based on degeneration and inflammation of nasal respiratory epithelium and hyperplasia of mucous secreting cells (LOAEL, 20 ppm [43 mg/m^3]) (U.S. EPA 1994). Sprague-Dawley rats (100/sex/group) were exposed to acrylonitrile concentrations of 0, 20, or 80 ppm 6 hours/day, 5 days/week for 2 years (U.S. EPA 1994). The effects observed included decreased body weights (males and females, 80 ppm); dose-related increase in water consumption (both sexes); increased mortality ($p<0.05$, males and females, both concentrations); and increased degenerative and inflammatory changes in the respiratory epithelium of the nasal turbinates ($p<0.05$, males and females, both concentrations). The nasal changes, more severe at 80 ppm, were characterized by suppurative rhinitis, hyperplasia, focal erosions, and squamous metaplasia (U.S. EPA 1994).

   Other studies have shown that acrylonitrile adversely affects animals exposed by inhalation. Animals inhaling acrylonitrile 4 hours/day, 5 days a week exhibited symptoms of toxicity at the concentrations and durations noted: guinea pigs (265 ppm for 8 weeks), rats (100 ppm for 8 weeks), and rabbits (100 ppm for 8 weeks) (U.S. EPA 1994). The effects included irritation of the eyes and nose, gastrointestinal disturbances, and weakness of the hind legs. The animals recovered after exposure ceased. More severe toxicity, including mortality, occurred in cats (153 ppm for 8 weeks), dogs (56 ppm for 4 weeks), and monkeys (153 ppm for 4 weeks). In a study designed to study it cancer-causing potential acrylonitrile concentrations of 60 ppm failed to induce adverse noncarcinogenic effects in Sprague-Dawley rats exposed 4-7 hours/day, 5 days/week for 104 weeks (U.S. EPA 1994).

   An oral reference dose (RfD) for acrylonitrile is currently under review by an EPA work group (U.S. EPA 1994).

D. Carcinogenicity

Long-term occupational exposure to acrylonitrile has been associated with cancer in humans. The U.S. EPA classifies acrylonitrile as a B1, probable human carcinogen.

1. Humans — Textile workers exposed to estimated concentrations of 5 to 20 ppm acrylonitrile were followed for 10 or more years (U.S. EPA 1994). In 1345 workers there were 25 cases of cancer, including five cases of respiratory cancer, all occurring among 1128 workers exposed for 6 or more months (SMR = 113). A trend of increased cancer incidence occurred with increased duration of exposure and increased length of follow-up time. The excess of respiratory cancer was statistically significant and persisted even when smoking was considered (5 observed, 1.6 expected).

   Statistically significant increased incidences of lung cancer were also observed in the following worker populations: 327 male workers at a rubber manufacturing plant employed 5 or more years; 1469 workers employed 6 months or more in acrylonitrile processing (increased incidences of tumors of the lymphatic system were also statistically significant); 934 men employed at least 1 year in polymerization of acrylonitrile and spinning acrylic fiber (increased incidences of stomach tumors were also statistically significant). These studies suffer from deficiencies in methodology, as do several other studies that reported no evidence of increased cancer incidence (U.S. EPA 1994).

   The U.S. EPA (1994) classifies acrylonitrile as a B1, probable human carcinogen, based on the observation of a statistically significant increase in the incidence of lung cancer in exposed workers and the observation of tumors (primarily astrocytomas in the brain) in rats of two strains by oral and inhalation routes of exposure. The oral slope factor for acrylonitrile is 5.4×10^{-1} per (mg/kg)/day; the drinking water unit risk is 1.5×10^{-5}

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[2]The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during the time period of concern.

per (micrograms/L); and the drinking water concentrations at specified risk levels are 6 micrograms/L (1 in 10,000), 6×10^{-1} micrograms/L (1 in 100,000), and 6×10^{-2} micrograms/L (1 in 1,000,000) (U.S. EPA 1994). The inhalation unit risk for acrylonitrile, based on respiratory cancer in humans, is 6.8×10^{-5} per (micrograms/m^3) and air concentrations at specified risk levels are 1.0 micrograms/m^3 (1 in 10,000), 1×10^{-1} micrograms/m^3 (1 in 100,000), and 1×10^{-2} micrograms/m^3 (1 in 1,000,000).

2. <u>Animals</u> — Acrylonitrile is carcinogenic to animals. AN induces increases in various types of tumors in Sprague-Dawley rats (unless another strain is noted) of either one or both sexes, under experimental conditions as summarized below (U.S. EPA 1994):

- in the drinking water at levels of 0, 35, 100, or 300 ppm administered to 48 rats/sex for 2 years; statistically significant increases in astrocytomas and in tumors of the Zymbal gland, stomach, tongue, and small intestine; generally dose-related;

- in the drinking water at levels of 0, 1, or 100 ppm; interim sacrifices performed at 6, 12, and 18 months (100/sex/group); the study was terminated early due to low survival rates; "significant" increases in the 100-ppm group for astrocytomas of the brain and spinal cord, carcinomas and adenomas of the Zymbal gland or ear canal, and squamous cell carcinomas and papillomas of the forestomach (note that this study was repeated in Fischer 344 rats [100/group] at doses of 0, 1, 3, 10, 30, or 100 ppm and increased incidences of astrocytomas and carcinomas of the zymbal gland [at $\geq$ 3 ppm] and mammary tumors in females [at 100 ppm] were observed);

- by gavage in olive oil 3 times/week for 52 weeks at doses of 0, or 5 ppm (40 treated and 75 control rats/sex); increased incidences of tumors of mammary gland and forestomach in females;

- orally administered at doses of 0, 0.10, or 10 mg/kg/day (70/sex/group; duration of exposure not clear, study terminated at 20 months); at high dose, statistically significant increased incidences of astrocytoma and tumors of the Zymbal gland, stomach and intestine (males), and mammary gland (females);

- 500 ppm in drinking water for three generations [strain CRL:COBS CD (SD) BR]; statistically significant increase in incidence of astrocytoma and cancer of Zymbal gland in second generation;

- inhalation of 0, 20, or 80 ppm 6 hours/day, 5 days/week for 2 years; statistically significant increase in tumors of central nervous system and other sites;

- inhalation of 0, 5, 10, 20, or 40 ppm 4 hours/day, 5 days/week for 12 months (30/sex/group); statistically significant increase in incidence of mammary tumors in males and skin carcinomas in females (concentrations at which tumors occurred were not stated).

E. Genotoxicity

Results of short term mutagenicity testing of acrylonitrile are mixed. The chemical was mutagenic in *Salmonella typhimurium* (with and without metabolic activation) and in *Escherichia coli* (with activation). It induced sister chromatid exchange in CHO cells and binds to DNA (U.S. EPA 1985; 1994). Acrylonitrile transforms Syrian hamster embryo cells and enhances the transformation of these cells infected with an oncogenic virus (U.S. EPA 1994). A likely metabolite of acrylonitrile, 2,3-epoxy-propionitrile (the 2-cyanoethylene oxide metabolite described in Section IV.B.3), is also mutagenic in *Salmonella* (U.S. EPA 1994).

Acrylonitrile did not induce chromosomal aberrations in bone marrow cells of rats and mice or in peripheral blood lymphocytes of exposed workers (U.S. EPA 1994). Acrylonitrile has been shown to increase DNA synthesis in rats (ATSDR 1990).

F. Developmental/Reproductive Toxicity

Exposure of pregnant animals to acrylonitrile orally or by inhalation results in developmental toxicity, including malformations. No information was found regarding the potential developmental toxicity of the chemical in humans. Under authority of Section 4 of the Toxic Substances Control Act) EPA has proposed additional testing of acrylonitrile for oral developmental toxicity in a species other than the rat.

1. <u>Humans</u> — No information was found in the secondary sources searched for the developmental/reproductive toxicity of acrylonitrile in humans.

2. Animals — Oral exposure of pregnant rats to 10, 25, or 65 mg acrylonitrile per kg/day by gavage resulted in a dose-related decrease in fetal body weight and increase in the incidence of delayed ossification and a variety of malformations (not described; these and the malformations observed in the inhalation study described below were "similar") (U.S. EPA 1991). The LOAEL for this study was 25 mg/kg/day, the NOAEL, 10 mg/kg/day.

   In a three-generation study, rats (15 males and 30 females/concentration) received 0, 106, or 522 ppm acrylonitrile in the drinking water ad libitum (U.S. EPA 1994). Parents of each generation were exposed for 100 days and throughout a 6 day mating period, gestation, and lactation. Exposure to 522 ppm acrylonitrile resulted in reduced viability and lactation indices ($p<0.05$) in all generations, and reduced water intake through lactation among dams of all generations. At 106 ppm, there were no changes in reproductive capacity, relative to controls (U.S. EPA 1994).

   Inhalation exposure of pregnant rats to 0, 40 or 80 ppm acrylonitrile vapors 6 hours/day during gestational days 6 to 15 resulted in maternal toxicity (at both concentrations) and fetal malformations ($p = 0.06$ at 80 ppm) that included short tail, missing vertebrae, short trunk, omphalocele and hemivertebrae (U.S. EPA 1994). Rats exposed to 40 ppm showed no signs of embryotoxicity or teratogenicity.

   Based on experimental deficiencies in the developmental toxicity testing of acrylonitrile and the high potential for exposure of workers and the general public to the chemical, the U.S. EPA (1991) (under section 4 of the Toxic Substances Control Act) has proposed additional testing of acrylonitrile for oral developmental toxicity in a species other than the rat (guideline requirements 40 CFR 798.4900; docket no. for OPTS, 42123/42124) (U.S. EPA 1991).

G. Neurotoxicity

The effects of acrylonitrile on the nervous system are similar to those of cyanide. Workers inhaling moderate levels of AN experienced headaches, apprehension, and nervous irritability. The effects in animals range from lethargy at moderate oral doses to paralysis at high inhalation concentrations.

1. Humans — The effects of acrylonitrile on the nervous system are similar to those of cyanide (ATSDR 1990). Workers exposed to acrylonitrile concentrations of 16 to 100 ppm for 20 to 45 minutes in a synthetic rubber manufacturing plant experienced headaches, feelings of apprehension, and nervous irritability (U.S. EPA 1994). A man accidentally sprayed with acrylonitrile suffered from dizziness and hallucinations (ATSDR 1990).
2. Animals — Dogs given acrylonitrile in oral doses of 16 mg/kg/day for 6 months exhibited depression and lethargy, and many died before the end of the study (ATSDR 1990). In another study in which dogs were given acrylonitrile in oral doses of 70 mg/kg/day for 1 to 2 years adverse effects included: decreased activity, abnormal gait, and prostration, but no deaths (ATSDR 1990).
   Dogs exposed to acrylonitrile by inhalation for 4 hours displayed excessive salivation at 30 ppm and paralysis of the hind limbs at 100 ppm (ATSDR 1990). Rats and dogs were exposed to acrylonitrile vapor concentrations of 25, 50, 75, or 100 ppm and monkeys were exposed to 75 ppm, all for 7 hours. The dogs were the most sensitive, showing anoxia-like histologic changes in the brain at levels of $\geq$50 ppm.

V. ENVIRONMENTAL EFFECTS

Acrylonitrile is moderately toxic to aquatic species, may produce toxicity and population effects in terrestrial species at high concentrations, and may contribute to smog formation.

A. Toxicity to Aquatic Organisms

Acrylonitrile is moderately toxic to most aquatic species exposed acutely. LC_{50} values in various species are as follows: 14.3 mg/L (96 hours) and 2.6 (30 days) for *Pimephales promelas* (fathead minnow); 24 mg/L (48 hours) for *Cyprinus carpio* (common carp); 33.5 mg/L (96 hours) for *Poecilia reticulata* (guppy); 10 mg/L (96 hours) for *Lepomis macrochirus* (bluegill); 5 mg/L (24 hours) for *Oncorhynchus mykiss* (rainbow trout); 7.6 mg/L (48 hours) for *Daphnia magna* (water flea); and 0.24 mg/L (24 hours) for *Lymnaea stagnalis* (snail, 100% mortality) (U.S. EPA 1985).

B. Toxicity to Terrestrial Organisms

No information was found in the available literature for the toxicity of acrylonitrile to terrestrial organisms. The oral LD_{50} value of 93 mg/kg for rats (ACGIH 1991) suggests that the chemical would not be acutely toxic to terrestrial animals unless present in moderate to high concentrations. Developmental toxicity has been noted in the fetuses of rats exposed to acrylonitrile (U.S. EPA 1994), suggesting that population effects may occur in animal species exposed to moderate to high concentrations in the environment.

C. Abiotic Effects

In a smog chamber, 5.3%/hour of the acrylonitrile disappeared (Howard 1989). For a first-order reaction, this is equivalent to a half-life of 13 hours. The products of the reaction were formaldehyde and PAN-type compounds.

VI. EPA/OTHER FEDERAL/OTHER GROUP ACTIVITY

The Clean Air Act Amendments of 1990 list acrylonitrile as a hazardous air pollutant. Occupational exposure to acrylonitrile is regulated by the Occupational Safety and Health Administration. The permissible exposure limit (PEL) is 2 parts per million parts of air (ppm) as an 8-hour time-weighted average (TWA) (29 CFR 1910). In addition to OSHA, other federal agencies and groups may develop recommendations to assist in controlling workplace exposure. The agencies and groups that should be contacted regarding workplace exposures or for additional information on acrylonitrile are listed in Tables 6 and 7.

TABLE 6. EPA OFFICES AND CONTACT NUMBERS INFORMATION ON ACRYLONITRILE

EPA Office	Statute	Contact Number
Pollution Prevention & Toxics	PPA[a]	(202) 260-1023
	EPCRA (§313/TRI)[b]	(800) 535-0202
	TSCA (§4)[c]	(800) 554-1404
Air	Clean Air Act (§111, 112B, 112R)[d]	(919) 541-0808
Solid Waste & Emergency Response	RCRA (Action levels:)[e] air, 1.00E-02 µg/m^3 water, 6.00E-05 mg/L soils, 1.00E-00 mg/kg	(800) 535-0202
	CERCLA (RQ, 100 pounds)[f]	(800) 535-0202
	SARA (§302A)	
Water	Safe Drinking Water Act	(800) 426-4791
	Clean Water Act (§304B, 307A, 311)[g] ao/dw. 0.059 µg/L ao, 0.66 µg/L	(202) 260-7588

[a]**PPA**: Pollution Prevention Act

[b]**EPCRA**: Emergency Planning and Community Right to Know Act of 1985

[c]**TSCA**: Toxic Substances Control Act

[d]**CAA**: Listed as hazardous air pollutant under §112 of Clean Air Act [42 U.S.C. 7401 et seq.]

[e]**RCRA**: Resource Conservation and Recovery Act. **Action Level**: health and environmental-based levels used by the EPA as indicators for the protection of human health and the environment and as triggers for a Corrective Measure Study.

[f]**CERCLA**: Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended. **RQ**: level of hazardous substance, which, if equaled or exceeded in a spill or release, necessitates the immediate reporting of that release to the National Response Center [40 CFR Part 302 (1991)] (U.S. EPA 1991).

[g]**Clean Water Act**: Clean Water Act. Regulates waters of the United States, including surface waters, ground waters, and wetlands [40 CFR Part 131 (1994)]. **ao/dw**: protection for consuming aquatic organisms and drinking water. **ao**: protection for consuming aquatic organisms.

TABLE 7. OTHER FEDERAL OFFICES/CONTACT NUMBERS FOR INFORMATION ON ACRYLONITRILE

Other Agency/Department/Group	Contact Number
American Conference of Governmental Industrial Hygienists (TLV-TWA, 2 ppm [4.3 mg/m^3]; skin; A2)[a]	(513) 742-2020
Agency of Toxic Substances & Disease Registry	(404) 639-6000
Consumer Product Safety Commission	(301) 504-0994
Food & Drug Administration	(301) 443-3170
National Institute for Occupational Safety & Health (TWA, 1 ppm; skin; Ca; LF)[b]	(800) 356-4674
Occupational Safety & Health Administration (TWA, 2 ppm[c]; ceiling, 10 ppm[d]) (Check local phone book under Department of Labor)	

[a]**TLV-TWA**: Time-Weighted-Average concentration for a normal 8-hr workday and a 40-hr workweek to which nearly all workers may be repeatedly exposed without adverse effects. **Skin**: air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required. **A2**: suspected human carcinogen (ACGIH 1993-1994).

[b]**TWA**: Time-Weighted-Average concentration for up to a 10-hour workday during a 40-hour workweek. **Ca**: potential human carcinogens. **LF**: Reduce exposure to lowest feasible concentration; when Ca designation accompanies lowest feasible designation, use of only the most reliable and protective respirators is recommended (NIOSH 1990, 1992).

[c]**TWA**: Time-Weighted-Average concentrations that must not be exceeded during any 8-hour work shift of a 40-hour workweek. **Skin**: air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required. OSHA standards promulgated pursuant to the Occupational Safety and Health Act, 29 CFR 1910 (OSHA 1993).

[d]**CEILING**: Airborne concentration that must not be exceeded as averaged over a 15-minute period during the work day.

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